REMARKS

By this Amendment, applicants have canceled claim 15 and amended claims 16, 23 and 24. No issue of new matter is raised by these amendments. Accordingly, applicants respectfully request that the Examiner enter and consider these amendments.

Priority

In the Final Office Action, the Examiner indicated that the claimed priority of PCT International Application PCT/IB03/05673, filed December 1, 2003 must be perfected in order for the subject application to have an effective filing date of the December 1, 2003. In response, applicants submit herewith an Application Data Sheet wherein such priority is claimed.

Rejection Under 35 USC § 112, Second Paragraph

The Examiner rejected claims 23 and 24 under 35 U.S.C. 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response, applicants have amended claims 23 and 24 to address the Examiner's concerns thereby obviating the Examiner's ground of rejection.

Rejection Under 35 USC § 102

The Examiner rejected claims 15-22 and 25-28 under 35 U.S.C. 102(e) as anticipated by Pacioretty and Babish.

In response, applicants first note that claim 15 has been canceled thereby rendering moot the Examiner's ground of rejection as to that claim. Applicants respectfully traverse the Examiner's rejection as to claims 16-22 and 25-28.

Applicants' invention as recited in amended claim 16 is directed to a method of treatment of lipodistrophy with an amount higher than or equal to 100 mg/day of DHA alone in a patient simultaneously submitted to antiretroviral therapy.

Pacioretty and Babish disclose a method of treating fat maldistribution resulting from anti-retroviral treatment of HIV-1 infection in a subject comprising administering a pharmaceutically effective dose of a docosahexaenoic acid in combination with a pharmacologically effective dose

of a thiol-containing compound or a bioavailable form of trivalent chromium. Pacioretty and Babish further disclose at paragraph 62 that preferably a daily dose of the present composition would be formulated to deliver about 0.05 to 20 g of conjugated fatty acid per day.

Applicants maintain that at least two differences exist between the subject-matter of claim 16 and that disclosed in Pacioretty and Babish. The cited prior art does not disclose the claimed invention wherein DHA alone is administered at an amount higher than or equal than to 100 mg/day to a patient concomitantly receiving anti-retroviral therapy is effective in the treatment of lipodistrophy. Accordingly, applicants maintain that Pacioretty and Babish does not disclose each and every element of claim 16 as now amended.

Pacioretty and Babish disclose that the combination of at least 2 ingredients: DHA and a thiol-containing compound or a bioavailable form of trivalent chromium, is the *one effective against fat maldistribution.* Pacioretty and Babish do not disclose, and nowhere can it be derived either explicitly nor implicitly, that *DHA alone* demonstrates this pharmacological and beneficial effect.

Moreover, paragraph 34 of Pacioretty and Babish states:

> "It should be noted that the phrase "conjugated fatty acid" or "conjugated fatty alcohol", as used herein, also includes isomers of fatty acids and fatty alcohols, as well as any other polyunsaturated compounds that act synergistically with sulfur-containing compounds and trivalent chromium complexes to promote fat maldistribution and decrease serum lipids in HIV/ART subjects. Suitable conjugated fatty acids include, without limitation, conjugated versions of linoleic acid, linolenic acid, gamma linolenic acid, arachidonic acid, mead acid, stearidonic acid, alpha-eleostearic acid, eleostearic acid, pinolenic acid, docosatetraenoic acid, 9, 12-octadecadienoic acid, octadecatrienoic acid, eicosatetraenoic acid, eicosapentaenoic acid, docosahexaenoic acid, docosapentaenoic acid, and all other diunsaturated and polyunsaturated fatty acids. In a preferred embodiment, the conjugated fatty acid is CLA in the triglyceride form." (Emphasis added)

This paragraph only asserts, without any experimental evidence for DHA, that such fatty acid in combination with sulfur-containing compounds and trivalent chromium complexes, experience an increase in potency when compared to each of the ingredients alone, which coordinated increase in potency is then useful "to promote fat maldistribution and decrease serum lipids in HIV/ART subjects".

"Synergism" is the interaction of discrete agents, elements, or constituents in such a way that the total effect is greater than the sum of the individual effects (Merriam-Webster Unabridged Dictionary). In terms of pharmaceutical *effective* benefits and in relation to synergism, the

meaning of synergism does not necessarily mean that the individual agents have sufficient potency alone to be effective pharmacologically. In the literature there are described several cases where ingredients alone are not sufficiently potent and must be administered in combination with another ingredient. Applicants maintain that the individual effects of DHA, and at which effective dose, are sufficient to fight fat maldistribution is not disclosed in Pacioretty and Babish.

In addition, Pacioretty and Babish disclose the combination of DHA and a thiol-containing compound or a bioavailable form of trivalent chromium to be administered to a patient with HIV/ART-related lipodystrophy, i.e. to a mixture of central or visceral fat accumulation that occurs following treatment with anti-retroviral therapies (see paragraph 27). Similarly, Pacioretty and Babish disclose a method of treating fat maldistribution resulting from anti-retroviral treatment of HIV-1 infection in a subject comprising administering a pharmaceutically effective dose of a docosahexaenoic acid in combination with a pharmacologically effective dose of a thiol-containing compound or a bioavailable form of trivalent chromium.

In contrast, applicants' claimed invention provides for the patient to be *concomitantly receiving* an active anti-retroviral therapy. Pacioretty and Babish disclose that the patient is treated for lipodistrophy *following* treatment with anti-retroviral therapies, not at the same time of the antiretroviral therapy.

In view if the remarks above, applicants maintain that Pacioretty and Babish do not anticipate claim 16 as now amended or claims dependent therefrom, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 USC § 103

The Examiner rejected claims 15, 23 and 24 under 35 U.S.C. 103 as obvious over Pacioretty and Babish.

In response, applicants again note that claim 15 has been canceled thereby rendering moot the Examiner's ground of rejection as to that claim. Applicants respectfully traverse the Examiner's ground of rejection as to claims 23 and 24.

As indicated above, Pacioretty and Babish does not teach each and every element of applicants' invention as recited in claim 16 as now amended from which claims 23 and 24 depend. The above-discussed differences are the type of matter: DHA alone versus a composition comprising

DHA and a thiol-containing compound or a bioavailable form of trivalent chromium, and the therapeutic regimen: DHA is co-administered with highly active antiretroviral therapy (HAART) versus DHA being administered after HAART.

Applicants maintains that the subject-matter of claim 16 as now amended is not obvious to one skilled in the art based on the disclosure of the cited prior art. One skilled in the art, when confronted with the teachings of Pacioretty and Babish, would be led away from trying DHA alone in the treatment of lipodistrophy. To the contrary, what the teachings by Pacioretty and Babish suggest is that the fatty acid alone is not sufficiently potent to combat fat maldistribution, since it needs to be administered with a second ingredient. Applicants' invention provided in claim 16 is a simplification over the prior art. This simplification is not only achieved in terms of ingredients but also in terms of therapeutic regimen. Treatment regimens in HIV infected patients are a priority issue in the industry since it is commonly acknowledged the problematic around the high amount of pills, timing, and schedules that the patient needs to manage. The co-administration of DHA with HAART is indeed an improvement in terms of quality of life for the patient. The administration of DHA alone is also a further improvement.

In view if the remarks above, applicants maintain that Pacioretty and Babish do not render obvious claims 23 or 24, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner also rejected claims 15-28 under 35 U.S.C. 103 as obvious over Holstein et al. in view of Connor et al.

In response, applicants again note that claim 15 has been canceled thereby rendering moot the Examiner's ground of rejection as to that claim. Applicants respectfully traverse the Examiner's ground of rejection as to claims 16-28.

Applicants respectfully disagree with the Examiner's interpretation of the cited prior art. Specifically, the Examiner interprets that hyperlipidemia is a form of lipodystrophy. Lipodystrophy is characterized by abnormal or degenerative conditions of the body's adipose tissue, i.e. abnormal fat distribution, and is particularly suffered by HAART patients. One of its most visible symptoms in HAART patients is facial fat loss, particularly in the cheeks. On the contrary, hyperlipidemia consists of the presence of raised or abnormal levels of lipids and/or lipoproteins in the blood. Hyperlipidemia usually has no noticeable symptoms and tends to be discovered during routine examination or evaluation for atherosclerotic cardiovascular disease.

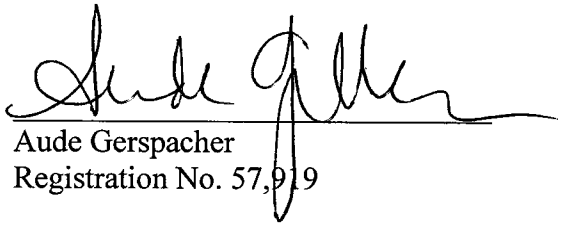
Connor et al. disclose the effect of dietary n-3 fatty acids from fish and fish oil in hypertriglyceridemic patients with combined hyperlipidemia (abstract). Being hyperlipidemia alone, or hypertriglyceridemia combined with hyperlipidemia, two clinical conditions different from lipodystrophy, there is no suggestion in Connor et al. that dietary n-3 fatty acids could be as well effective in lipodystrophy. Accordingly, applicants maintain that it was certainly not obvious for the skilled in the art, when departing from the teachings of Connor et al, that the administration of DHA would be for example effective in increasing facial fat loss. As a matter of fact, there are yet no drugs currently approved for the treatment of lipodystrophy.

In view if the remarks above, applicants maintain that Holstein et al. in view of Connor et al. do not render obvious claim 16 as now amended or claims dependent therefrom, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Reconsideration and allowance of all the claims herein are respectfully requested.

Respectfully submitted,

April 2, 2008



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